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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,634	02/19/2002	Paul Habermann	02481.1774	2606

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ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER

DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/076,634

Applicant(s)

HABERMANN ET AL.

Examiner

Patricia A. Duffy

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7-14, 16-21 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 9-14, 16-21 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The arguments and translation documents filed 10-4-04 have been entered into the record. The amendment to the title filed 10-6-04 has not been entered into the specification, as it is not in compliance with 37 CFR 1.121. The amendment to the claims filed 1-5-05 has been entered. The amendment to the title and specification filed 5-31-05 have been entered. Claims 6, 15 and 22 have been cancelled. Claims 7 and 8 are withdrawn from consideration. Claims 1-5, 9-14, 16-21 and 23-25 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

This application contains claims 7 and 8 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Objections/Rejections Withdrawn

The use of the trademarks at least at pages 3, 4, 15 and 23 have been noted in this application.

Priority

The examiner acknowledges the English-language translation and a statement that the translation is accurate of the provisional application 60/270,593.

Claims 1-6 and 9-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection as to claim 1 and every claim dependent thereon is withdrawn in view of Applicants' amendment to the claim.

The rejection in relation to claim 6 is withdrawn in view of the cancellation of the claim.

The rejection of claim 14 and every claim dependent thereon is withdrawn.

The rejection as to claims 15, 16 and 17 is withdrawn in view of the amendment to claim 14.

The rejection as claims 19, 20 and 23 is withdrawn in view of the amendments.

The rejection of claim 21 is withdrawn in view of the amendment to the claims.

Rejections Maintained

Double Patenting

Claim 1-6 and 9-23 of this application conflict with claims 1-3 and 7-20 of Application No. 10/076,631 and claims 1-3 and 7-20 of Application No. 10/076,632. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Applicants' response of 5-31-05 is still non-responsive on this issue. This is not a double patenting issue but a conflicting claims issue involving multiple prosecutions of similar inventions.

Claims 1-6 and 9-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 7-20 of copending Application No. 10/076,631. Although the conflicting claims are not identical,

they are not patentably distinct from each other because the specifically claimed and disclosed species anticipate the instantly claimed invention is maintained for reasons made of record in the office action mailed 6-16-04.

Applicants' response notes the provisional double patenting rejections would be addressed upon the indication of allowable subject matter. No indication of allowable subject matter will be made until such time as Applicants distinguish the inventions or file an appropriate disclaimer.

Claims 1-6 and 9-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 7-20 of copending Application No. 10/076,632. Although the conflicting claims are not identical, they are not patentably distinct from each other because the specifically claimed and disclosed species anticipate the instantly claimed invention is maintained for reasons made of record in the office action mailed 6-16-04.

Applicants' response notes the provisional double patenting rejections would be addressed upon the indication of allowable subject matter. No indication of allowable subject matter will be made until such time as Applicants distinguish the inventions or file an appropriate disclaimer.

Claims 1-6, 9-14, 16-21 and 23-25 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons made of record and herein.

Applicant arguments have been considered but are not persuasive. Applicants acknowledge the claimed genus encompasses widely variant structure and indicate that the Examples provide for adequate written description. This is not persuasive. Applicants argue that "S" can be any signal sequence. This is not persuasive because applicants argue in the response that it has to have the additional property of increasing yields and neither the specification nor the art define the structural feature of a signal peptide that provides for this function. As to "F", F is specifically defined in the specification to indicate that allows secretion of a protein encoded by Y into a fermentation medium. In contrast to Applicants assertion, hirudin or its derivatives or variants have not been demonstrated to have this property. A signal sequence "S" allows for secretion of a protein into a fermentation medium. Every single Example of the specification and the art from which the plasmids were derived, have signal sequences. This specification fails to teach that hirudin or the derivative has the functional property of allowing secretion. There is no teaching in the specification that provides for an expression construct limited to hirudin or derivative thereof provides for secretion. In other words, hirudin or derivative thereof itself has not been demonstrated in any host cells to be recombinantly produced as a secreted product, absent more. Applicants argue Examples 1-9, the nucleic acid of claims are not so structurally limited. This is the issue here with the definition of "F" in the specification. Further, the specification does not define hirudin derivatives and therefore provides for unlimited variation of hirudin. The exemplification of two known N-terminal substitutions and lepirudin in the Examples does not provide adequate written description of a genus of unlimited variation.

Claim 1-6, 9-14, 16-21 and 23-25 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particularly disclosed nucleic acids encoding fusion proteins, plasmids, bacterial host cells and methods of fermentative production in a bacterial cell and isolation of the fusion proteins thereof

from a culture supernatant as particularly set forth in the Examples of 1-9 of the specification, it does not reasonably provide enablement for the claimed nucleic acids encoding fusion proteins, plasmids, host cells, methods of making and purification is maintained for reasons made of record.

Applicants argue that the amendments obviate this rejection. This is not persuasive; the claims are not limited to the particularly disclosed nucleic acids etc. Examples 1-9 provide for particulars that are not set forth in the independent claims. For example, the amendment did not address the issue of hirudin or derivatives thereof as allowing for or directing secretion into a culture cell medium and isolation from a supernatant. All of the examples provide for a particular nucleic acid, a particular signal sequence and defined host cell (*E. coli*) to get production into the culture medium. As indicated, there is no evidence of record that the nucleic acid of claim 1 is either expressed or secreted. Applicants have simply not provided any evidence of such in any of the relied upon Examples. As such, this rejection is maintained in its entirety, as Applicants have not particularly addressed any of the issues set forth herein.

Claims 1-5, 9-14, 16-21 and 23-25 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 3, the following phrases have no meaningful interpretation "smompa derived from", "ecoompc derived from", "af009352 derived from", "aeoynta derived from" or "stomps1 derived from" because these acronyms apparently represent specifically claimed nucleic acid sequences not described nor specifically defined in the specification. Applicants argue that the specification specifically defines these sequences at paragraphs 128-131, page 28 of the specification. This is not persuasive; the specification does not define these terms to be limited to the specific nucleic acids, but provides exemplification by parentheses. Further, the specification does not indicate by language "By this we mean

that and only that". As such, the description does not convey a limited definition of these terms and sequences encompassed. Limitations of specific sequences of particular database genes are not read into the claims, because databases can be revised, modified or eliminated. As such, Applicants argument of a definition is not persuasive.

As to claim 4, the recitation of "Ser-hirudin" or "Ala-hirudin" have no meaningful interpretation in view of the specification because the specification does not describe nor define what these apparent variants are or are intended to encompass. Applicants argue that the specification teaches that the variants different in structure by a number of amino acids at page 1, paragraph 2. Applicants arguments are not persuasive, the passage that Applicants rely upon is not present at page 1, paragraph 2. Further, since applicants define variants in that the different in structure by a number of amino acids, it is not clear that these variants are the structures of the prior art where the N-terminus is substituted or varied. Given the lack of definition of derivative and the definition of variant in the specification to encompass any substitution, insertion or deletion in variation, the claimed terms are not seen as limited to the commercial embodiments or to the N-terminal derivatives of the art. As such, the metes and bound are still indefinite in view of the teachings of the specification. Further, Applicants amendment now includes natural isoforms (that are specifically included in the definition of "hirudin" (see page 40). As such, the term hirudin derivative is necessarily seen to include hirudin as defined in the specification. Therefore, the skilled artisan would not be readily apprised as to the metes and bounds of the claimed derivatives.

As to claim 17, the claim recites precipitation components of a culture medium, however, no culturing step in culturing medium is provided for in the previous claims. Use of the phrase "components of a culture medium" is not provided for. Applicants' amendments do not obviate this issue.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine

the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. Applicants argue that "signal sequence" is used in its conventional meaning but the additional property of increasing yield is an additional property. This is not persuasive; the art does not define the structure of any signal peptide that provides for the alleged additional functional additional property. Therefore, given any random signal sequence, the skilled artisan would be unable to ascertain whether or not that the signal sequence has the asserted additional property as to be included or excluded by the claims.

Claims 1, 2, 6, 9-15, 17, 22 and 23 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dawson et al, WO 91/09125 published 27 June 1991 is maintained for reasons made of record in the Office Action Mailed .

Dawson et al teach a nucleic acid encoding a promoter-signal peptide-hirudin-cleavable linker-hirudin-enhancer or nucleic acid encoding a promoter-signal peptide-hirudin-cleavable linker-streptokinase-enhancer in plasmids contained in host cells (see Examples 1-15) and methods of production therefrom, isolation of the fusion from supernatants and cleavage of linker and release of active streptokinase and hirudin in *E. coli* and *S. cerevisiae*. As such, the claims are anticipated by the prior art.

The rejection is maintained for reasons made of record, in view of the lack of definition of "hirudin derivative" and its specific inclusion of natural isoforms in claim 4. Applicants' arguments that a hirudin is not a hirudin derivative is inconsistent with the amendment of the claims and specific variants included within the definition of "hirudin" in the specification as filed.

New Rejections Based on Amendment

New Rejections

Claims 1-5, 9-14, 16-21 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 1 and 24 and every claim dependent thereon, the term hirudin derivative is not defined in the specification as such the skilled artisan would not be apprised of the metes and bounds of this term. Further, the use of "derivative" is confusing because the specification at page 4 indicates that the natural hirudin isoforms as set forth in claim 4 are specifically denoted as "hirudin" in the specification and therefore the term "hirudin derivative" encompasses natural hiruidins. As such, the metes and bounds of this term cannot be ascertain because it is unclear how one of skill in the art distinguished derivatives of hirudin that are meant to be included within the scope of the term as opposed to those derivative of hirudin that are n not included within the scope of the claim.

As to claim 14, 21 and every claim dependent thereon, claims 14 and 21, now recite, "fermenting the host cell of claim 11 in a fermentation medium resulting in a fermentation supernatant". The process of fermentation does not provide fermentation "supernatant" or a "fermentation medium". Supernatant is a clear liquid overlaying material deposited by settling, precipitation or centrifugation. As such, there is no supernatant isolated. The fermentative process provides for both. There is no step that provides for supernatant isolation from the host cell. The process as defined is clearly inconsistent with the defined meanings of the art. Further it is unclear from what the fusion protein is isolated and it is unclear what "produced thereby" references. Applicants' amendment removed this issue from claim 18 and inserted it into claim 14. As such, this issue has not been resolved by the amendment and is not applicable to claims 14, 16-21 as amended.

Status of Claims

Claims 1-5, 9-14, 16-21 and 23-25 stand rejected. Claims 7 and 8 are withdrawn from consideration.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to

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reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Pat A. Duffy
Patricia A. Duffy

Primary Examiner

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